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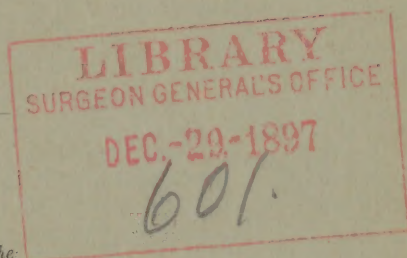
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T. L. (Case Series K, No. 61, 1895), aged thirty-one years; male; laborer; admitted to the Presbyterian Hospital May 30, 1895.

Family history: Father and mother both died of alcoholism; two sisters living and well. Family history otherwise unknown.

Previous history: The patient has had the usual diseases of childhood. He worked on a farm since he was seven years old. He had malaria fifteen years ago; typhoid fever four years ago, followed by dropsy of the legs. Soon after recovery he contracted gonorrhœa.

History of present disease. March, 1895, the patient had a severe attack of influenza, when he suffered from severe pain in the loins and legs. The pains persisted, and in May of the same year he applied to the hospital for treatment of the pain, and on account of a movable tumor which he accidentally discovered in his left side, and which gave him pain when reclining on that side. When questioned he stated he was weaker than usual, and that he had lost some flesh and had irregular abdominal pains.

Condition on admission: Patient was a white man, of moderate height, and weighed one hundred and sixty pounds. The skin and mucous membranes were of good color. The countenance was bright. The pupils were normal, and reacted to light and distance.

The chest was well formed. The respiratory movements were shallow and rapid, but nothing abnormal was found on physical examination. The apex-beat of the heart was in normal position. A soft systolic murmur not transmitted was heard at the apex and at the aortic cartilage. The cardiac dulness was not increased. The pulse was slow, of fair strength and volume. The artery wall showed slight evidence of endarteritis.

The abdomen was distended, and on palpation a tumor could be distinctly outlined occupying the position of an enlarged spleen. The lower edge was painful; the right border extended to the median line, and the lower border to within an inch of the ilium. The splenic dulness extended from the eighth rib to the transverse umbilical line, and in the anterior axillary line

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was twelve inches in length. Dulness extended from the xyphoid cartilage to the left eight inches in a direct line, and from the umbilicus to the lumbar muscles. The upper limit of liver-dulness was normal; the lower border extended one inch below the costal margin; the edge could be felt. The abdomen measured thirty-four inches at the umbilicus.

With the exception of the afore-mentioned weakness and the hurried breathing there were no other subjective symptoms. The appetite was good, the bowels regular, and there was no indigestion. The urine contained no albumin or sugar, nor abnormal elements under microscopical examination.

June 11, 1895, the abdomen measures thirty-three inches, and the length of the spleen is ten inches. The edges can easily be palpated. The left leg has been swollen and tender during the past week. The blood-examination shows hæmoglobin 34 per cent., red blood-corpuscles 4,000,000, white blood-corpuscles 57,200.

The patient remained in the hospital until the 10th of August. He gained in strength to a remarkable degree. The abdomen was reduced to thirty-one inches in circumference, but the spleen remained about the same. During July the inguinal glands became enlarged and painful, and during both June and July the left leg was more or less œdematous, and the seat of pain. When the patient was discharged the white blood-corpuscles numbered 300,000; the red blood-corpuscles 4,100,000. Notwithstanding the increase in strength the patient lost ten pounds in weight. His temperature was normal, the pulse ranged between 80 and 90, and the respirations 20 and 26 per minute.

Readmitted December 25, 1895, suffering from the symptoms enumerated above, although greatly intensified, particularly the pain in the left hip and abdomen. Both legs are œdematous and there is œdema of the trunk in moderate degree. The patient is not as strong, but has not lost much flesh.

On physical examination the face and hands are observed to be reddened, and there is a marked flush on each cheek. The remainder of the body is pale and waxy as in anasarca. The radial arteries are extremely atheromatous. This change and the occurrence of anasarca are the most marked objective signs. The systolic murmur at the apex is more pronounced, and is transmitted into the axilla. The upper limit of liver-dulness is normal, but extends an inch below the costal margin, where it is palpable. The spleen is larger than on the previous examination. The epigastric region is dull on percussion due to the enlarged left lobe of the liver and the encroachment of the spleen. There is a large amount of ascites. The hæmoglobin is 30 per cent.; red blood-corpuscles 3,000,000; white, 640,000.

The patient died on the 7th of February. During the month of January the anasarca became extreme. The temperature ranged from $96\frac{2}{3}^{\circ}$ to $99\frac{1}{2}^{\circ}$, the pulse between 84 and 120, and the respirations 24. There were several attacks of epistaxis. From the day of the last admission there was painless diarrhœa, with stools containing mucus and occasionally blood. Death took place suddenly. He awakened from sleep with a sharp cry, and was imme-

diately afterward found semi-conscious. Frothy blood and mucus were discharged from the mouth, and death took place in a few moments.

Autopsy. A portion of the body only could be examined. The tissues in the abdominal cavity were nearly filled with serum. The pleural cavities were about one-fourth full of fluid, and the pericardium contained six ounces. The heart was flabby, the muscle pale, the left ventricle half an inch thick. The right ventricle contained a light-green clot. A small green clot was seen on the mitral valve. The aortic valves were thickened, and there were spots of atheroma on the aorta.

The left lung was œdematous, and the lower part collapsed. The right lung was in the same condition. At the apex evidences of old tubercle were seen. The large bronchi were filled with bloody froth. The lymphatic glands in the mediastinum and the roots of the lungs were enlarged, gray, and succulent. The spleen was ten and a half inches in length; weight 990 grammes. It was firm, chocolate colored, and mottled with fine dark spots. Malpighian bodies not prominent. Liver, weight 3320 grammes; greatest breadth fourteen and a half inches. On close inspection fine irregular streaks were seen running throughout on section. Thyroid gland apparently normal. Pancreas normal; nothing unusual in the appearance of the stomach. In the large intestine throughout its whole extent there were many large serpiginous ulcers. In the lower portion of the ileum there were four irregular punched-out ulcers. The rectum was the seat of ulceration. The upper part of the small intestine was injected in spots, but there were no hemorrhages or petechiæ. All of the abdominal glands were enlarged, especially those about the gastro-hepatic omentum. They were of a light-greenish tinge, and very succulent. The spinal cord was removed for examination. Brain not examined.

The Blood. The blood of the patient was examined on the 30th of January of this year and found to contain 1,571,875 erythrocytes and 382,188 leucocytes per cubic millimetre, or a proportion of one white to four red cells.

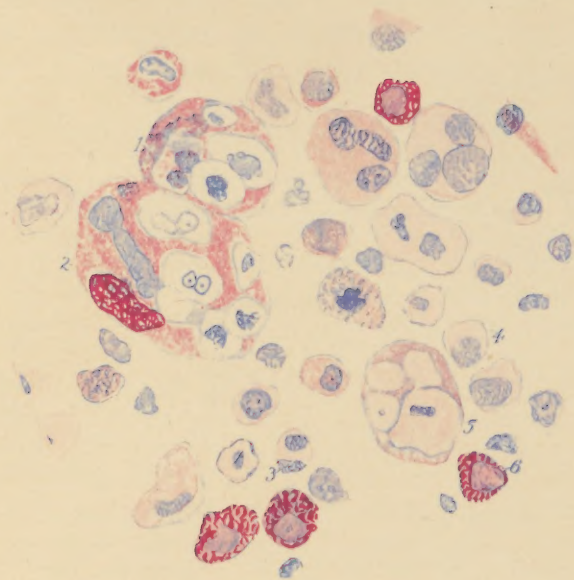
In order to determine the specific gravity, a picnometer holding about 6 grammes was filled with blood taken from the median vein of the forearm; the result was 1049.88; and as the percentage of error of this method is very slight, the result may be taken as fairly accurate.

Chemical examination. The blood from the picnometer was then boiled for about twelve hours in the presence of a great excess of ammonium sulphate, filtered, and the filtrate examined by the usual method for *peptone*. The characteristic reaction occurred, but as a recent thorough investigation of this method by Dr. Caspar Miller has led him to believe that it does not positively exclude the albuminoses, we cannot assert that peptone was certainly present. Certain other compounds, however, that have been described in leucæmic blood—that is, xanthin, hypoxanthin, lactic and acetic acids, and acetone—were absent from the specimen examined. The determination of the degree of alkalinity and of the proportion of the fibrin-forming elements could not, unfortunately, be made. The former because of the lack of appa-

ratus at the hospital, the latter because the withdrawal of the considerable amount of blood required by the Bleibtreu method, about 100 c.c., was considered unjustifiable in the serious state of the patient.

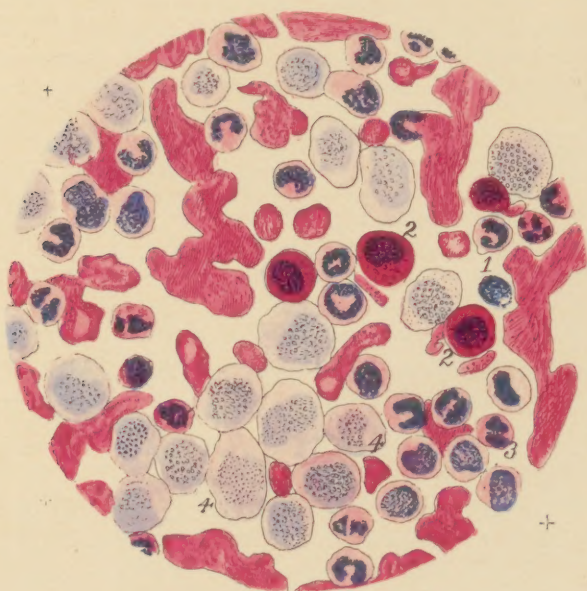
Microscopical examination. A number of cover-glass preparations were made and fixed, either by heat, or the ether-alcohol mixture. The latter were stained in the usual way with hæmatoxylin and eosin. The most characteristic feature of the blood so prepared was the presence of a large number of leucocytes from two to three times the size of a red cell, containing a single round nucleus, either eccentrically placed, or, less commonly, in the centre. This nucleus usually took the stain poorly, appearing as a pale blue disc, while the protoplasm of the cell had a faint purplish tinge. There were also a number of mononuclear cells, slightly smaller on the average than the first-mentioned group, whose nuclei stained deeply, quite as well as those of the polynuclear cells. Very often these nuclei were irregular and belonged to the transitional type, but as every gradation existed, it was thought best not to attempt to separate them. A third form consisted of large irregular cells with large nuclei, staining very poorly, and a colorless protoplasm without a very distinct boundary, that appeared to be granular. These cells were three or four times larger in diameter than the red blood-cells. The proportion of all these mononuclear elements to the whole number of leucocytes was 66.2 per cent. As nearly as could be determined, 10 per cent. of all the mononuclear elements belonged to the last type described.

Another group of mononuclear cells was the ordinary lymphocytes with the small deeply staining nucleus and the narrow rim of protoplasm; of these there were but 0.8 per cent. The ordinary polynuclear elements of the blood formed 24.4 per cent. of the total number of leucocytes. The eosinophil cells could be divided into three groups, the mononuclear and polynuclear forms, with deeply staining nuclei and coarse, closely packed granula, and certain mononuclear cells, with large pale nuclei and rather finer, more scattered granula. Sometimes these granula were dispersed as if the cell had burst during the smearing. In each group of fields containing 1000 leucocytes, 19.8 nucleated red blood-cells were found, a proportion to the whole number of erythrocytes of about 0.47 per cent. It now remained to determine the proportion of mononuclear cells containing neutrophilic granula. The preparations fixed by heat, for some unknown reason, for other preparations fixed at the same time and in the same manner were excellent, refused to stain well by the ordinary aniline mixtures, such as Biondi's or Rosin's stains or the mixtures containing basic fuchsin. The best success was obtained with a mixture suggested by Dr. A. E. Taylor, containing methylen-blue, methyl-green, neutral red and orange. Counts made of preparations stained by this method showed that 62 per cent. of the mononuclear elements contained neutrophilic granula. These cells were composed largely of the smaller cells with dark nuclei, that varied from the round to the transitional type; but besides these, the neutrophilic granula were found in the large cells with the pale irregular nuclei. These latter



Lymph-gland, retroperitoneal region. Hardened in alcohol;
Rosin's stain. $\times 1500$.

1. Globiferous cell. 2. Globiferous cell containing polynuclear and eosinophile cells. 3. Polynuclear cell. 4. Mononuclear cell. 5. Globiferous cell. 6. Eosinophile cell.



Blood-leucemia. Hematoxylin and eosin.

1. Lymphocyte. 2. Eosinophile cell (mononuclear). 3. Polynuclear leucocyte. 4. Large mononuclear leucocyte (myelocyte?).

may be taken to correspond to the myelocytes of Ehrlich, for, although the absence of amœboid movement was not determined, they agreed in the other characteristics.

Differential count. To summarize the results, then, there were:

<i>Erythrocytes</i>	80 per cent.
Of these there were	
Nucleated	0.47 "
<i>Leucocytes</i>	20 "
Of these	
Mononuclear elements	66.2 "
Polynuclear elements	24.4 "
Eosinophil cells	8.6 "
Lymphocytes	0.8 "

Microscopical examination of the tissues. When the patient died Dr. Hughes kindly provided pieces of the lung, liver, spleen, kidney, pancreas, lymph glands, and a small section of the radius. The study of these specimens is not yet complete, as some of the methods of fixing and hardening require more time than has been at our disposal, and, very unfortunately, a piece of the bone that was rapidly decalcified was spoiled in the process, so that as far as the bone-marrow is concerned, perhaps the most important of all, it can only be said that no peculiar changes can be detected. It contains considerable fat and cells of various sizes, some of them containing the oxyphil granula. The lymph glands were not especially enlarged, one from the bronchial region contained considerable black pigment. In all were found numerous cells with oxyphil granula. A peculiar feature was the presence of enormous polynuclear cells. One of the larger of these measured not less than $31\frac{1}{2}$ by 35 microns. In the substance of these cells were found broken-down red blood-cells, some pigment, and apparently leucocytes. They contained a number of nuclei, relatively small and scattered; the outline was fairly regular. They showed particularly well in sections stained with Rosin's mixture, the nuclei appearing a bright green and the protoplasm taking a faint reddish tinge.

In appearance these cells strongly suggest the giant-cell of sarcoma. But it is to be observed that they correspond very closely to the description of the globiferous cell described by Biondi in Ziegler's *Beitrage*, Band xviii., Heft 1. Moreover, the presence of degenerated cells in the midst of the protoplasm marks them as unquestionably phagocytic in their nature, and although Biondi's article is unfortunately not illustrated, it seems reasonable to conclude that these cells are the same as those found by him in his experimental work with toluyl-endiamin. It is perhaps permissible to draw the inference that, if active cell-destruction is taking place in the lymph glands, the fact is

favorable to the theory that they are not the primary seat of the disease. A further proof of this cellular disintegration is to be found in the preparations stained by Quincke's method for iron, in which numerous cells are found that stand out sharply from the general background.

The spleen shows increase of the lymphoid elements, and a certain amount of hyperplasia of the connective tissue. As in the glands, the number of oxyphil cells appears to be large, and there are in addition certain large cells with one or more small nuclei and a protoplasm that has a strong affinity for the acid stain; but, unlike the eosinophil cells, stains with a uniform color. One of these cells measured $17\frac{1}{2}$ by 42 microns. The reaction of the protoplasm shows that they are probably degenerating, and perhaps they represent a late stage of the globiferous cells. It appears, therefore, that in this tissue, also, cellular destruction is taking place. Many of the cells, as in the glands, contained distinct traces of iron.

The parenchymatous elements of the pancreas exhibited considerable degenerative changes; the nuclei stained poorly and the cells were swollen and irregular; there was also a considerable excess of connective tissue.

The eosinophile cells found in the tissues fixed by picric acid and stained with Gollasch's mixture showed beautiful chromatine figures, and in many of them the nuclei contained nucleoli, none were found with karyokinetic figures.

The other organs showed characteristic leucæmic infiltration: the liver was slightly fatty; the kidney showed here and there a partial obliteration of the space between the glomerulus and its capsule, but was, on the whole, in excellent condition. The lungs presented a peculiar feature. The alveoli were filled with a substance that appeared to be homogeneous, stained deeply with the acid stains, and was partially adherent to the epithelium. It could not be celloidin, for that takes the basic aniline colors, and probably represents a coagulated exudate, but its exact nature we have not determined.

The symptoms and course of the disease were not unusual. With the exception of moderate enlargement of the lymphatic glands of the groin during life these structures did not appear to be involved, and were excluded as pathological factors in the leucæmia. From the physical examination and the results of the examination of the blood during life, we considered the leucæmia was of myelogenic and splenic origin. The histological findings appear to show the bone-marrow was not affected, while the lymphatic glands had undergone the changes peculiar to leucæmia, and that the disease was, contrary to our belief, of the splenic and lymphatic variety. It seems, therefore, that the blood examination does not suffice to distinguish the types.

The case was one of lymphatic and splenic leucæmia notwithstanding the blood did not indicate that the lymphatic glands were affected during life.

In the histological study of the tissues attention is called, first, to the globiferous or giant-cell in the lymphatics, which are undoubtedly phagocytic. Second, to the iron found in the tissues, showing that blood-destruction must have been in progress. Both conditions point to an infectious process. The occurrence of the extensive intestinal ulceration not leucæmic, with the histological findings, seems to indicate that a process somewhat allied to that in pernicious anæmia was present, either from the beginning of the disease or set in, the result of a terminal infection.

SUMMARY.

Clinical. Weakness, lumbar pain, and the accidental discovery of a tumor in a male aged thirty-four years. Enlargement of the spleen, anæmia and leucocytosis, enlarged inguinal glands, great anasarca, occasional epistaxis, colitis. Blood showed evidence of disease of bone-marrow.

Anatomical. The internal organs showed changes seen in leucæmia. *Iron* in the tissues. Phagocytes or globiferous cells in the glands. A further report will be made on the histological structure of the spinal cord. The urine should have been submitted to a quantitative examination.

